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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
08/962,094	10/31/1997	PATRICIA A. BILLING-MEDEL	5995.US.P1	8450

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STEVEN F. WEINSTOCK
ABBOTT LABORATORIES
100 ABBOTT PARK ROAD
DEPT. 377/AP6A
ABBOTT PARK, IL 60064-6008

EXAMINER	
SITTON, JEHANNE SOUAYA	
ART UNIT	**PAPER NUMBER**
1634	

DATE MAILED: 11/26/2003

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	08/962,094	BILLING-MEDEL ET AL.	
	Examiner	Art Unit	
	Jehanne Souaya Sitton	1634	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133).
- Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *28 July 2003*.

2a)☒ This action is **FINAL**. 2b)☐ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *80-84* is/are pending in the application.

4a) Of the above claim(s) *84 and 85* is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *80-83* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☒ Claim(s) *80-84* are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. §§ 119 and 120

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

13)☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. § 119(e) (to a provisional application) since a specific reference was included in the first sentence of the specification or in an Application Data Sheet. 37 CFR 1.78.

a) ☐ The translation of the foreign language provisional application has been received.

14)☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. §§ 120 and/or 121 since a specific reference was included in the first sentence of the specification or in an Application Data Sheet. 37 CFR 1.78.

Attachment(s)

1) ☐ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO-1449) Paper No(s) _____ .
4) ☐ Interview Summary (PTO-413) Paper No(s). _____ .
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: .

DETAILED ACTION

Election/Restrictions

1. Newly submitted claims 83 and 84 are directed to an invention that is independent and distinct from the invention originally claimed for the following reasons: Claims 83 and 84 ~~and 85~~ are drawn to detecting a polypeptide (Group III, see Restriction requirement mailed 3/25/1999) which is independent and distinct from a method of detecting nucleic acids (Group I, see Restriction requirement mailed 3/25/2003) which is the invention elected in the response filed April 26, 1999.

Since applicant has received an action on the merits for the originally presented invention, this invention has been constructively elected by original presentation for prosecution on the merits. Accordingly, claims 84 and 85 are withdrawn from consideration as being directed to a non-elected invention. See 37 CFR 1.142(b) and MPEP § 821.03.

2. Claims 80-84 are newly added in the instant application. Claims 1-79 have been cancelled. Claims 83 and 84 are withdrawn from consideration as being drawn to non elected invention. All the amendments and arguments have been thoroughly reviewed but are deemed insufficient to place this application in condition for allowance. Any rejections not reiterated are moot in view of applicant's cancellation of the claims. The following rejections are newly applied to claims 80-82, necessitated by amendment. They constitute the complete set being presently applied to the instant Application. This action is FINAL.

Claim Objections

3. Claims 80-82 are objected to because of the following informalities: Claim 80 lacks either a modifier "a" before the recitation of 'breast cell', or the term "breast cell" should be plural. Claim 81is grammatically incorrect in the recitation, in lines 7-8, of "detection of a BS106 gene product is detected in the sample". Claim 82 contains a misspelling, the term "in" should be "is". Appropriate correction is required.

Claim Rejections - 35 USC § 112

4. The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

5. Claims 80-82 are rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the written description requirement. The claim(s) contains subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention. This is a NEW MATTER Rejection.

The claims recite methods of detecting a breast cell or a breast malignancy by taking a sample of tissue other than breast tissue and detecting if a BS106 gene product is present. This constitutes new matter because the specification does not provide support for a method of detecting a breast cell in a sample taken from tissue other than breast tissue, or of detecting a malignancy of breast tissue by determining if a BS106 gene product is present in non breast tissue.

A thorough review of the specification reveals that the specification contemplated methods of detecting BS106 in a sample, (see page 28, line 20); generally detecting BS106 (see pages 22-23), detecting breast cancer by detecting BS106 (page 11, line 16), and detection of the marker in blood, plasma, or serum (page 88, line 1) body fluids (page 88, line 4). The specification generally contemplates that the marker may be elevated in a disease state, altered in a disease state, or be a normal protein in an inappropriate body compartment (page 88, lines 6-7). However, such disclosure does not specifically support a method of detecting a breast cell in a sample taken from *any* tissue other than breast or for a method of detecting a malignancy of breast tissue by providing a sample from *any* non breast tissue and determining if a BS106 gene product is present, the presence of such being indicative of breast cancer. For example, RNA blots in figure 3a using BS106 probes indicate expression in normal breast and cancerous prostate (see lane 7). However, the specification provides no contemplation that the expression in cancerous prostate is either an indication of a breast cell in that tissue or of a breast malignancy. Further, the recitation of "a normal protein in an inappropriate body compartment" does not provide specific support for the protein being in a breast cell, but encompasses secreted protein in an inappropriate body compartment. Consequently, this amendment has introduced new matter into the claims.

6. Claims 80-82 are rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the enablement requirement. The claim(s) contains subject matter which was not described in the specification in such a way as to enable one skilled in the art to which it pertains, or with which it is most nearly connected, to make and/or use the invention.

There are many factors to be considered when determining whether there is sufficient evidence to support determination that a disclosure does not satisfy the enablement requirements and whether any necessary experimentation is undue (See *In re Wands,* 858 F. 2d 731, 8 USPQ2d 1400, 1404 (Fed. Cir. 1988)). These factors include, but are not limited to:

Quantity of Experimentation Necessary
Amount of Direction and Guidance
Presence and Absence of Working Examples
Nature of the Invention
Level of predictability and unpredictability in the art

The claims are broadly drawn to a method of detecting a breast cell in a sample taken from tissue other than breast tissue by determining if a BS106 gene product is present in the sample, the presence of such indicating the presence of a breast cell and a method of detecting a malignancy o f breast tissue, the method comprising providing a sample from non breast tissue of a human and determining if a BS106 gene product is detected in the sample, the presence of a BS106 gene product being indicative of a breast malignancy.

The term "BS106" is broadly defined in the specification, for example, the specification teaches at page 10, lines 30-31 that a "BS106 gene" or a fragment thereof is DNA which can have minimally 50% identity to SEQ ID NO: 4. Therefore, the claims also broadly encompass detection of a sequence that has minimally 50% identity to SEQ ID NO: 4 being indicative of the presence of a breast cell in a tissue other than breast tissue, as well as a breast malignancy. The term "BS106" is not an art recognized term and thus the prior art is silent with respect to structural and functional features that may be used to ~~identity~~ identify such polynucleotides. Further, the specification does not teach that a nucleic acid that has minimally 50% identity to any of SEQ ID NOS 1-5 is specific for breast cells. As such, the specification does not teach a) that the presence

of a breast cell in a sample other than breast tissue can be detected by detecting any nucleic acid that has minimally 50% identity to any of SEQ ID NO: 1-5, or b) that a breast malignancy can be detected by detecting a nucleic acid that has minimally 50% identity to any of SEQ ID NOS: 1-5.

The claims additionally are broadly drawn to a method of detecting a malignancy wherein the presence of a "BS106 gene product" in a tissue sample other than breast is indicative of a breast malignancy. The specification teaches that SEQ ID NOS 1-3 are overlapping clones that result in a consensus sequence of SEQ ID NO: 4 (see page 55). The specification teaches that SEQ ID NO: 4 was compared to an EST database and was found in 85.7% of breast libraries and only .2% of non breast libraries. The specification teaches that total RNA was obtained from solid breast tissue and from non-breast tissue and used for Northern Blot analysis and RT-PCR. Figures 3A and 3B show results of a Northern Blot analysis using SEQ ID NO: 1 as a probe with RNA from normal breast tissue, normal prostate and cancerous prostate (3A) and from normal breast and cancerous breast tissue (3B). However, the figures show that the probe hybridized to all normal breast, a prostate cancer sample, and only 2 out of 6 breast cancer samples. Therefore, from such data it is clear that the mere presence of a "BS106" gene product is not indicative of a breast malignancy as SEQ ID NO: 1 showed hybridization in normal breast and cancerous prostate samples. Furthermore, nowhere does the specification contemplate or disclose that the expression of SEQ ID NO: 1 in the cancerous prostate was indicative of a breast malignancy. While Table 1 indicates that overexpression corresponding to hybridization with SEQ ID NO: 1 occurred in two malignant breast samples, table 1 also shows that expression on the order of expression in normal breast was found in one malignant breast sample, and that in a second malignant breast sample, no expression was found. Therefore, the specification fails to

establish that overexpression of SEQ ID NO: 1 is indicative of breast malignancy. It is further noted that the specification does not contemplate or disclose a method of detecting a breast malignancy by detecting a BS106 gene product or nucleic acid such as DNA or RNA in *any* non breast tissue.

Therefore, given the lack of guidance in the specification or the art as to a method of detecting a breast cell in a sample of non breast tissue by detecting a 'BS106 gene product" or a method of detecting a breast malignancy by detecting a "BS106 gene product" in any non breast tissue, the skilled artisan would be required to perform undue experimentation to practice the invention as claimed. Firstly, the specification provides no evidence that a nucleic acid with minimally 50% sequence identity to any of SEQ ID NOS 1-5 is specifically expressed only in breast cells. Further, as noted in the rejection made in section 5 above, and reiterated in the instant rejection, the specification does not specifically teach or contemplate a method of detecting a breast malignancy by detecting a BS106 gene product in *any* non breast tissue. Furthermore, the specification has not established that either the mere presence of BS106 in any tissue sample, including breast, or the overexpression of BS106 in any sample, including breast, is predictably associated with breast malignancy. Therefore, a large amount of trial and error analysis, the results of which are unpredictable, would be required of the skilled artisan to determine if any sequence which minimally only has 50% identity to any of SEQ ID NOS: 1-5 would be diagnostic of either the presence of a breast cell or a breast malignancy in any non breast tissue sample. Given the minimal disclosure in the specification, and the lack of any teaching in the art, it would further be unpredictable if the presence of BS106 in any non breast

tissue sample was indicative of a breast malignancy. As such, the experimentation required by the skilled artisan to make and use the invention is considered undue.

In the response dated 5/6/2002, a declaration by Dr. Paula Friedman, under 37 CFR 1.132 was submitted. The Declaration provided data showing that the results of experiments conducted on lymph node tissue from breast cancer patients and non breast cancer patients to detect the presence of BS106 RNA. The results show that detection of BS106 is correlated to detection of metastatic breast cells in lymph nodes. However, the declaration fails to provide evidence that the claims were enabled *at the time of filing of the instant application* because the specification has only described the use of BS106 for detecting breast tissue and breast cancer by detecting BS106 in breast tissue. The specification does not describe or contemplate testing lymph nodes for the presence of breast cancer cells using a BS106 polynucleotide. The specification does not provide any teaching that BS106 was specifically contemplated to be associated with metastatic breast tumors, but instead asserts its association to breast cancer in breast tumors from *breast tissue*. As stated in In re Glass, 181 USPQ 31, (CCPA 1974), "if a disclosure is insufficient as of the time it is filed, it cannot be made sufficient, while the application is still pending by later publications which add to the knowledge of the art so that the disclosure, supplemented by such publications, would suffice to enable the practice of the invention. Instead, sufficiency must be judged as of the filing date." The fact that the specific method encompassed by claims 80-82 is not disclosed in the specification indicates that the specification does not support the claims, but instead reflects further critical information that was discovered after the application was filed, and is essential for the artisan to practice the invention.

Conclusion

7. Applicant's amendment necessitated the new ground(s) of rejection presented in this Office action. Accordingly, **THIS ACTION IS MADE FINAL.** See MPEP § 706.07(a). Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the date of this final action.

8. No claims are allowable.

9. Any inquiry concerning this communication or earlier communications from the examiner should be directed to examiner Jehanne Sitton whose telephone number is (703) 308-6565. The examiner can normally be reached Monday-Thursday from 8:00 AM to 5:00 PM and on alternate Fridays.

Note: The examiner's name has changed from Jehanne Souaya to Jehanne Sitton. All future correspondence to the examiner should reflect the change in name. It is also noted that after January 12, 2004, the examiner will be located at the new USPTO campus and will be reachable at telephone number (571) 272-0752.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Gary Jones, can be reached on (703) 308-1152. The fax phone number for this Group is (703) 872-9306.

Any inquiry of a general nature should be directed to the Group receptionist whose telephone number is (703) 308-0196.

Jehanne Sitton

Jehanne (Souaya) Sitton
Primary Examiner
Art Unit 1634

11/25/03